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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/258,217	02/26/1999	MARK T. KEATING	2323-127	3509

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WASHINGTON, DC 20005

EXAMINER

CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 09/11/2003

32

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/258,217

Applicant(s)

KEATING ET AL.

Examiner

Shin-Lin Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 2 is/are allowed.
- 6) ☒ Claim(s) 3-5, 9 and 10 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' amendment filed 7-14-03 has been entered. Claims 1-5, 9 and 10 have been amended. Claims 1-5, 9 and 10 are pending and under consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 3 and 4 remain under 35 U.S.C. 103(a) as being unpatentable over Keating, 1997 (Cardiovascular research, Vol. 36, p. 134-137, IDS-AB) in view of Wydner et al., 1994 (X2) and is repeated for the reasons set forth in the preceding Official action mailed 1-7-03 (Paper No. 30). Applicant's arguments filed 7-14-03 have been fully considered but they are not persuasive.

Applicants argue that Keating does not teach knocking out elastin gene but rather teaches knocking out candidate gene that is contiguous to the elastin gene and that there is no motivation

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to make knockout mouse in which the elastin gene is knocked out (amendment, p. 5). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-7-03 (Paper No. 30). Although it is not necessary that the candidate gene is the elastin gene, however, Keating teaches that "SVAS is a common feature of Williams syndrom, we hypothesized that mutations involving the elastin gene might also be responsible for this disorder. Mutational analyses of familial and sporadic cases indicated that WS was indeed associated with submicroscopic deletions of chromosome 7q11.23: inherited or de novo constitutional deletion of one elastin allele was identified in every WS patient studied" (see p. 136, left column, first paragraph). Since Keating teaches making mice having targeted knockout of the candidate gene to study the phenotype of said mice, one of ordinary skill would have been motivated to make mice having knocked out elastin gene to study the phenotype of said mice. Thus, claims 3 and 4 remain rejected under 35 U.S.C. 103(a).

4. Claims 5, 9 and 10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reitamo et al., 1994 (V) in view of Keating, 1997 (Cardiovascular research, Vol. 36, p. 134-137, IDS-AB) in view of Wydner et al., 1994 (X2) and is repeated for the reasons set forth in the preceding Official action mailed 1-7-03 (Paper No. 30). Applicant's arguments filed 7-14-03 have been fully considered but they are not persuasive.

Applicants argue that there is no motivation to make a transgenic mouse having knockout of the elastin gene and William's syndrom involves more than just the elastin gene such that there is no motivation to use patient with William's syndrome to test drugs for treating SVAS. Applicants further argue that there is no suggestion in Reitamo to detect effect of the cytokine in

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a human or mouse model for SVAS (amendment, p. 5, 6). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-7-03 (Paper No. 30) and the reasons set forth above. Although William's syndrome may involve more than just the elastin gene, it is clear that mutations involving the elastin gene is associated with SVAS and SVAS is a common feature of WS patient as taught by Keating. Therefore, one of ordinary skill in the art would have been motivated to use WS patient to test drugs for treating SVAS. Reitamo teaches a method of screening a compound which can stimulate the elastin promoter *in vivo or in vitro*. IL-10 is a compound that was shown to be able to up-regulate elastin gene expression in vivo or in vitro. Since mutations involving the elastin gene is associated with SVAS and SVAS is a common feature of WS patient, it would have been obvious for one of ordinary skill to use the WS patient having one deleted elastin gene and the mouse cells having only one functional elastin gene to screen for drugs or compounds useful for treating humans with SVAS, hypertension or atherosclerosis which are diseases associated with arteries.

Conclusion

Claims 3-5, 9 and 10 are rejected. Claims 1 and 2 are in condition for allowance.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

A handwritten signature in black ink, appearing to read 'Shin-Lin Chen', is located in the lower right quadrant of the page.